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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/572,522	BERGMANN, ANDREAS	
	Examiner	Art Unit	
	CHIH-MIN KAM	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 March 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/21/07;5/21/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. In the preliminary amendment filed March 21, 2006, claims 4-6 and 8 have been amended, and claim 10 has been cancelled. Therefore, claims 1-9 are pending and examined.

Informalities

The disclosure is objected to because of the following informalities:

2. The specification recites an amino acid sequence, TPDVS at page 12, line 7, however, this sequence does not have sequence identifier "SEQ ID NO:" and is not listing in the Sequence Listing. If this sequence is part of SEQ ID NO:1, it can be indicated as "amino acid residues X to Y of SEQ ID NO:1". Appropriate correction is required.

Claim Objections

3. Claims 2, 3, 5, 6 and 8 are objected to because the claims use quotation marks, which should be avoided in the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of diagnosing a disease in a patient comprising determining the content of apolipoprotein C-I in a serum or plasma sample of the patient, and comparing the content of apolipoprotein C-I of the patient with those of normal healthy persons, wherein content of apolipoprotein C-I of the patient is reduced as compared to those of normal healthy

persons, and wherein the disease is sepsis; and for a method of determining apoC1 level in the blood sample of sepsis patient as shown in the art, does not reasonably provide enablement for a method for the diagnosis, early detection, risk estimation and monitoring of the course of diseases, wherein the content of apolipoprotein C-I and/or of derivatives thereof is determined in a serum of plasma sample from a human patient and the presence of a disease is concluded on the basis of a result of the determination which differs significantly from the value range determined for normal healthy persons, when the derivatives of apolipoprotein C-I, the variation for the content of apolipoprotein C-I between patient's plasma and plasma of healthy controls, and the diseases are not defined. The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-9 are directed to a method of for the diagnosis, early detection, risk estimation and monitoring of the course of diseases comprising determining the content of apolipoprotein C-I in a serum or plasma sample from a human patient as compared to values obtained from normal healthy persons. The specification, however, only discloses cursory conclusions without data supporting the findings, which states that the present invention relates to a determination of apolipoprotein C-I as a biomarker for the diagnosis of diseases such as sepsis or cancer (pages 4-6). There are no indicia that the present application enables the full scope in view of the claimed methods as discussed in the stated rejection. The present application does not provide sufficient teachings to enable the full scope of the claims. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the

breadth of the claims, the absence or presence of working examples, the state of the prior art and relative skill of those in the art, the predictability or unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding the derivatives of apolipoprotein C-I, the variations of content of apolipoprotein C-I between patients' plasma and healthy persons' plasma, and the diseases, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

The specification shows that fractions of the total apolipoprotein C-I present in blood samples of patients with various diseases are determined by their binding to hydrophobic molecular structures (e.g., octylsepharose chromatography materials; Figs. 1 and 2; pages 9-11), and the data indicate in the samples from sepsis patients, tumor patients, patients with manifest/acute cardiac diseases (Ci, Ape, AOD) and patients with Crohn's disease, significantly reduced values of apolipoprotein C-I are found as compared with healthy persons. For patients with diabetes type I and type II, reduced values of apolipoprotein C-I are also found, although not to the same extent (Figs. 2a, 2b and 2c). The specification also use an immunoassay of the sandwich type to determine apolipoprotein C-I content in serum or plasma samples of sepsis and tumor patients, for sepsis samples, the measurements confirm the results of the chromatographic investigation, where significantly reduced values were obtained as compared with normal persons (pages 13-15; Fig. 4). However, for tumor samples, there was a tendency for the measured values to be increased (Fig. 4), which differs from the results obtained from

chromatographic investigation (Fig. 2a). While the specification discusses the results from two determinations, the chromatographic and immunodiagnostic investigations (pages 16-17), it appears that only sepsis samples have significantly reduced values of apolipoprotein C-I as compared with normal persons.

(3). The state of the prior art and relative skill of those in the art:

While the related art (e.g., Rensen *et al.* (US 2006/0111283 A1)) teaches patients having sever sepsis exhibit strongly lowered apoC1 level in their blood samples using a sandwich Enzyme-Linked immunoSorbent Assay, the art does not teach monitoring the apoC1 level in patients having other diseases. Thus, the specification needs to provide specific guidance on monitoring the apolipoprotein C-I content in the plasma samples of patients having various diseases, to be considered enabling for the claimed method associated with the variants.

(4). Predictability or unpredictability of the art:

The claims are directed to a method of for the diagnosis, early detection, risk estimation and monitoring of the course of diseases comprising determining the content of apolipoprotein C-I in a serum or plasma sample from a human patient as compared to values obtained from normal healthy persons. While the specification shows plasma samples of sepsis patients have significantly reduced values of apolipoprotein C-I as compared with normal persons in both chromatographic method and immunoassay, the measurements of apolipoprotein C-I for tumor patients obtained from two methods are not consistent. Since chromatographic method only determines fractions of the total apolipoprotein C-I that bind to hydrophobic molecular structures, and immunoassay determines the total apolipoprotein C-I, when the measurements of apolipoprotein C-I obtained from two methods are not consistent (e.g., for tumor samples), it is

not clear how to use apolipoprotein C-I measurement of the patient's plasma sample for diagnosis or monitoring of the course of disease.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method of for the diagnosis, early detection, risk estimation and monitoring of the course of diseases comprising determining the content of apolipoprotein C-I in a serum or plasma sample from a human patient as compared to values obtained from normal healthy persons. While the specification discloses plasma samples of sepsis patients have significantly reduced values of apolipoprotein C-I as compared with normal persons in both chromatographic method and immunoassay, it does not disclose the measurements of apolipoprotein C-I in plasma for patients with various diseases as compared to those of healthy controls using immunoassay. When the measurements of apolipoprotein C-I obtained from two methods (i.e., chromatographic method and immunoassay) are not consistent (e.g., tumor samples), it is not clear how to use apolipoprotein C-I measurement of the patient's plasma sample for diagnosis or monitoring of the course of disease. Since the specification does not provide sufficient teachings on the use of apolipoprotein C-I measurement in the claimed method, it is necessary to carry out undue experimentation to identify the effect of apolipoprotein C-I in various diseases.

(6). Nature of the Invention

The scope of the claims encompasses determining apolipoprotein C-I content in the method of diagnosing or monitoring the course of diseases, but the specification does not provide

the sufficient teachings on the use of apolipoprotein C-I measurement in the claimed method. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, the working example does not demonstrate the claimed methods in associated with variants, the effects of apolipoprotein C-I in various diseases are unpredictable, and the teachings in the specification are limited, therefore, it is necessary to carry out undue experimentation to identify the effect of apolipoprotein C-I in various diseases.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claims 1-9 are indefinite because of the use of the term "derivatives thereof". The term cited renders the claim indefinite, it is not clear what structure the derivative of apolipoprotein C-I has and how different the derivative is from its parent peptide. Claim 1 also recites the term "in a serum of plasma sample", it is not clear what it means. Claims 2-9 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

7. Claims 1-9 are indefinite because of the use of the term "differs significantly", "significantly reduced", "significantly changed", "high probability" or "deviate significantly".

The term cited renders the claim indefinite, it is not clear what is the mete and bounds for the cited term since they are all relative terms. Claims 2-9 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

8. Claim 6 recites the limitation "the cause of a cancer disease" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim.

9. Claim 7 is indefinite because it recites the word “vaue”, it is not clear what the word means.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Barlage *et al.* (J. Lipid Research Vol. 42, 281-290 (February 2001), cited in the IDS filed 1/21/2007).

Barlage *et al.* teach 2D-GGE of plasma samples obtained from healthy individuals and septic patients were performed and it showed apoC-I immunoreactivity decreased in the septic patients as compared with healthy control subjects (page 286, left column; Fig. 6; page 288, left column, second paragraph; claim 1 and 4).

11. Claims 1, 3 and 4 are rejected under 35 U.S.C. 102(e) as being anticipated by Rensen *et al.* (US 2006/0111283 A1, PCT filed 6/27/2003; cited in the IDS filed 5/21/2008).

Rensen *et al.* teach patients having sever sepsis exhibit strongly lowered apoC1 level in their blood samples, where the apoC1 level is determined with a sandwich Enzyme-Linked immunoSorbent Assay (sandwich ELISA) (paragraphs [0026], [0036], [0049], [0065], [0073]-[0078]; Fig. 1; claims 1, 3 and 4).

Conclusion

12. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached at 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Chih-Min Kam/
Primary Examiner, Art Unit 1656

CMK
July 14, 2010